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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,964	07/06/2000	KEITH B HOFFMAN	THUR-001	4643

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EXAMINER	
WANG, SHENGJUN	
ART UNIT	**PAPER NUMBER**
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/582,964	HOFFMAN ET AL.	
	Examiner	Art Unit	
	Shengjun Wang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43,46,47,51 and 54-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43,46,47,51 and 54-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of applicant's amendments and remarks submitted January 22, 2007 is acknowledged.

Claim Rejections 35 U.S.C. 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43, 46, 47, 51, 54-58, 62-65 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claimed methods are directed to a method of treating epilepsy, by administering a serine protease inhibitor. First, there is lack of written description as to the serine protease inhibitors in general. As noted in pages 6 to 7 in the specification, there are many kinds of proteases. The application provides written description to some of the protease inhibitors, but fails to provide sufficient written description commensurate with the scope herein claimed. Applicants merely define those ligands by their function, not by their structures. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: the vice of a functional claim exists not only when a claims is wholly functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty. Functional language at the point

of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate. Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first or second paragraph. Claims employing functional language at the point of novelty, such as Applicants, neither provide those elements required to practice the inventions, nor inform the public during the life of the patent of the limits of the monopoly asserted *General Electric Company v. Wabash Appliance Corporation et* supra, at 468.

It is note that the application does not define the genus of "serine protease inhibitors" or by structure, or by structure in conjunction with specific functional characteristics. The particular examples herein are distinct each from the others in their chemical structures. One of skilled artisan would not be able to envision the other "serine protease inhibitor" which would be useful in the claimed invention. The instant specification fails to provide descriptive information, such as definitive structural or function features of the claimed genus of "serine protease inhibitors" that would distinguish the claimed "serine protease inhibitors" from other molecules with the similar properties. Since the disclosure fails to describe the common contributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of certain "serine protease inhibitors" is insufficient to describe the genus. *Vas-Cath Inc. v. Mahurkar,* 19 USPQ 2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purpose of the 'written description' inquiry, whatever is now

claimed." (see page 1117). The specification does not "clearly allow person of ordinary skill in the art to recognize that [he or she invented what is claimed." (see Vas-Cath at page 1116). As discussed above, by reading the specification herein, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of serine protease inhibitors.

2. Claims 43, 46, 47, 51, 54-58 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for employ those protease inhibitors disclosed at pages 6-7 in the specification, does not reasonably provide enablement for other compounds which may function as serine protease inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The claimed invention define the compounds employed therein solely by its function, encompassing any compounds that may function as serine protease inhibitors. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to In re Wands, 8 USPQ 2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factor to consider when assessing if a disclosure would have required undue experimentation. The court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

7) the predictability of the art, and

8) the breadth of the claims.

The claim recites the employment of serine protease inhibitors. The application does not define the genus of "serine protease inhibitors" or by structure, or by structure in conjunction with specific functional characteristics. The particular examples herein are distinct each from the others in their chemical structures. One of skilled artisan would not be able to envision the other "serine protease inhibitor" which would be useful in the claimed invention. The instant specification fails to provide descriptive information, such as definitive structural or function features of the claimed genus of "serine protease inhibitors" The state of the prior art indicates that it is unpredictable as to the structures of serine protease inhibitors. Applicants fail to provide information allowing skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "serine protease inhibitors" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed of physiological activity. The instant claims read on all "serine protease inhibitors", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention, absent undue experimentation.

Additionally, claims 51, 54, 56-58, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph because applicants fail to set forth the criteria that define those situations wherein this pathology, epilepsy, could be prevented. Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these situations without undue experimentation. The

claims read on preventing all type onsets of epileptic seizures, particularly status epilepticus, a life threatening condition in which the brain is in a state of persistent seizure See page 1370 in The Merck Manual of record. In the instant case, no examples is set forth illustrating a situation where epilepsy is prevented, thereby failing to provide sufficient working examples. It is noted that these examples are not exhaustive. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In the instant case, it is known in the art that many underline etiologies may cause epilepsy. There is no single drug known in the art can control all type s of seizures. See, e.g., The Merck Manual, pages 1366-1375. The instant claims read on preventing all type of epileptic seizure activity necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 55 and 57 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. The term "like" in claims 55 and 57 is a relative term, which renders the claim indefinite. The term "like" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention. The claims are indefinite as to the serine protease encompassed thereby.

Claim Rejections 35 U.S.C. 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 43, 46, 47, 51, 54-58 are rejected under 35 U.S.C. 102(e) as being anticipated by Strickland et al. (US 5,786,187, IDS).

8. Strickland et al. teach a method of treating, suppressing or preventing seizure, and/or epilepsy in human or animal by inhibiting the activity of serine protease, particularly, with a tPA inhibitor. See, particularly, column 1, lines 55 to column 2, line 9, column 3, lines 17-28, column 11, lines 21-48 and the claims.

Claim Rejections 35 U.S.C. 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 43, 46, 47, 51, 54-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strickland et al. (US 5,786,187, IDS) and in further view of Citron et al.

11. Strickland et al. teach a method of treating, suppressing or preventing seizure, and/or epilepsy in human or animal by inhibiting the activity of serine protease, particularly, with a tPA inhibitor. See, particularly, column 1, lines 55 to column 2, line 9, column 3, lines 17-28, column 11, lines 21-48 and the claims.

12. Strickland does not teach expressly the employment of AEBSF as the inhibitor or the particular amounts herein.

13. However, Citron at al teaches that AEBSF is an old and well-known broad-spectrum serine protease inhibitor, and is particularly useful in neuron cell protection. See, particularly, the abstract.

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed the invention was made, to use AEBSF as the inhibitor in Strickland's method for treating patients with epilepsy.

A person of ordinary skill in the art would have been motivated to use AEBSF as the inhibitor in Strickland's method for treating patients with epilepsy because AEBSF is an old and well known broad spectrum serine protease inhibitor, and would have reasonably expected to be effective in inhibiting tPA, a serine protease. As to the particular function recited in claim 59, it is noted that a chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990. See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product. As to the effective amounts recited in claim 61, note the optimization of a result effective parameter, e.g., effective amount of

a therapeutical agent, is considered within the skill of the artisan. See, In re Boesch and Slaney (CCPA) 204 USPQ 215.

Claims 62-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strickland et al. (US 5,786,187, IDS), for reasons set forth above, and in further view Ben-Ari et al. and the Merck Manual, page 1370.

Claims 62-65 require that epilepsy is associated with sprouting, or the epilepsy is status epilepticus. Ben-Ari et al discloses that sprouting is known to be associated with epilepsy. See, particularly the abstract. The Merck Manual shows that status epilepticus is one type of epilepsy.

It is noted that Strickland et al. do not teach expressly the epilepsy is associated with sprouting or is status epilepticus.

However, it would have been obvious to treat that particular epilepsy since the method of Strickland is disclosed as generally useful for treating epilepsy and seizure. One of ordinary skill in the art would have been reasonably expected the method of Strickland be useful for treatment of the particular type of epilepsy and/or seizure as Strickland et al. do not particularly limit the method to any particular type of epilepsy or seizure.

Response to the Arguments

Applicants' amendments and remarks submitted January 22, 2007 have been fully considered, but are not persuasive.

14. As to the rejections under 35 U.S.C. 112, first paragraph, applicants argue that "serine protease inhibitor" is known in the art, and the application provides many examples. The examiner recognizes that "serine protease inhibitor" is merely understood as functional description of compounds capable for inhibiting serine protease. As revealed in the application,

there are many kinds of proteases, some of them have known inhibitors and others may not. Each of those protease and corresponding inhibitors have acquired a separate status in the art of treating as a separate subject matter for inventive effect as evidenced by the numbers of patents recited in the application. Furthermore, the scope as claimed encompass any compounds possessing functional properties that have not been discovered or recognized by the artisan.

2. AEBSF is a recognized broad-spectrum serine protease inhibitor. However, one may not make a reasonable extrapolation from this single compound to any serine protease inhibitors since there are many kinds of serine proteases and inhibitors. Note it is understood that not all serine protease inhibitors have the broad inhibiting activity as AEBSF. Further, the specification merely shows it is tPA that is released to extracellular synaptic space which results in the proteolysis of neuronal CAMs (pages 17). The application provide no rationale that how inhibitors of other serine protease would be effective in the claimed method. It is an undue experimentation for one of ordinary skill in the art to explore if other inhibitors are indeed effective for the method as herein claimed. Note since AEBSF is known for broad spectrum of activity, the evidences showing that AEBSF is similarly active as some other compounds is some particular aspects do not support that the other compounds would have the same activities as required by the claimed invention.

3. As to the rejections of claims 51, 54, 56-58, it is note that the claims are directed to "preventing on set seizure." "Preventing on set seizure" are construed as to encompass completely stop the on set seizure with 100% assurance. The animal model employed in the application is reasonably valid for screening agents that would reduce the frequency or suppress

the severity of the on set seizure, but has not been established as a model for agents that can completely keep seizure from happening.

4. As to the rejections under 35 U.S.C. 112, second paragraph, applicants contend that "trypsin-like" is a phrase that has been frequently used in the art. However, being frequently used is not a standard fro a clear scope. The issue is whether there is art-recognized standard for identifying a protease as trypsin-like vs. no trypsin-like. The application, or any evidence on the record, has not established such a standard.

Applicants traverse the rejections based on Strickland simply because Strickland does not actually administer a serine protease inhibitor to treat a host for epilepsy. Applicants' arguments are untenable. Applicants essentially argue the inoperability of Strickland reference. Since every patent is presumed valid (35 U.S.C. 282), and since that presumption includes the presumption of operability (Metropolitan Eng. Co. v. Coe, 78 F.2d 199, 25 USPQ 216 (D.C.Cir. 1935), examiners should not express any opinion on the operability of a patent. Strickland et al. expressly teach and claim a method of treating, suppressing or preventing seizure, and/or epilepsy in human or animal by inhibiting the activity of serine protease, particularly, with a tPA inhibitor.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Wang

Shengjun Wang
Primary Examiner
Art Unit 1617

SHENGJUN WANG
PRIMARY EXAMINER